BY

ZeeReelSubterranean

Target-Specific Binding and Functional Activity of 1-Amino-3,5-dimethyladamantane HCl

Target-Specific Binding and Functional Activity of 1-Amino-3,5-dimethyladamantane HCl

Compiled by ZeeReelSubterranean

(Edited: 2025-04-15T09:54:48Z)

Target	System	Value (Kᵢ and IC₅₀, nM; IP, %)	Metric	Action	Species	Location	Ref.
NMDA (MK-801 site)	Glutamatergic	540 1250 690 6700 700 433 5600 1730 1370 7600 1320 2420 7300 1780 6500 1400	K_i IC_{50} K_i IC_{50} K_i K_i IC_{50} K_i K_i IC_{50} K_i K_i IC_{50} K_i IC_{50} IC_{50}	Non-competitive/uncompetitive antagonist	Human Human Rat Rat Rat Rat Rat Rat Rat Rat Rat Rat Rat Rat Rat Rat Rat	Frontal cortex Embryonic kidney cells Cortex Frontal cortex Cerebellum Striatum Striatum Parietal cortex Hippocampal CA1 subfield Hippocampal CA1 subfield Hippocampal CA3 subfield Hippocampal DG subfield Hippocampal DG subfield Striatum Entorhinalcortex Cerebellar granule cell layer	Kornhuber, J., Bormann, J., Hübers, M., Rusche, K., & Riederer, P. (1991). Effects of the 1-amino-adamantanes at the MK-801-binding site of the NMDA-receptor-gated ion channel: A human postmortem brain study. *European Journal of Pharmacology: Molecular Pharmacology*, *206*(4), 297–300. https://doi.org/10.1016/0922-4106(91)90113-V Kotermanski, S. E., Wood, J. T., & Johnson, J. W. (2009). Memantine binding to a superficial site on NMDAreceptors contributes to partial trapping. *The Journal of Physiology*, *587*(19), 4589–4603. https://doi.org/10.1113/jphysiol.2009.176297 Bresink, I., Danysz, W., Parsons, C. G., & Mutschler, E. (1995). Different binding affinities of NMDA receptor channel blockers in various brain regions—Indication of NMDA receptor heterogeneity. *Neuropharmacology*, *34*(5), 533–540. https://doi.org/10.1016/0028-3908(95)00017-Z Porter, R. H. P. & Greenamyre, J. T. (1995). Regional variations in the pharmacology of NMDA receptor channel blockers: Implications for therapeutic potential. *Journal of Neurochemistry*, *64*(2), 614–623. https://doi.org/10.1046/j.1471-4159.1995.64020614.x
NMDA (Superficial site)	Glutamatergic	58,900–99,300	IC_{50}	Weak non-competitive antagonist	Human	Embryonic kidney cells	Kotermanski, S. E., Wood, J. T., & Johnson, J. W. (2009). Memantine binding to a superficial site on NMDAreceptors contributes to partial trapping. *The Journal of Physiology*, *587*(19), 4589–4603. https://doi.org/10.1113/jphysiol.2009.176297
GluD2	Glutamatergic	1% at 1 μM	IP	Weak inhibitor	African clawed frog	Oocytes	Williams, K., Dattilo, M., Sabado, T. N., Kashiwagi, K., & Igarashi, K. (2003). Pharmacology of δ2 glutamate receptors: Effects of pentamidine and protons. *Journal of Pharmacology and Experimental Therapeutics*, *305*(2), 740–748. https://doi.org/10.1124/jpet.102.045799
σ_1	Sigmaerguc	2600 4180	K_i K_i	Weak agonist	Rat Rat	Forebrain Cerebellum	Peeters, M., Romieu, P., Maurice, T., Su, T.-P., Maloteaux, J.-M., & Hermans, E. (2004). Involvement of the sigma$_1$ receptor in the modulation of dopaminergic transmission by amantadine. *European Journal of Neuroscience*, *19*(8), 2212–2220. https://doi.org/10.1111/j.0953-816X.2004.03297.x
D_2^{High}	Dopaminergic	137 917	K_i K_i	Agonist	Chinese hamster Rat	Ovary cells Striatum	Seeman, P., Caruso, C., & Lasaga, M. (2008). Memantine agonist action at dopamine D_2^{High} receptors. *Synapse*, *62*(2), 149–153. https://doi.org/10.1002/syn.20472
5-HT$_3$	Serotoninergic	2290 2200	IC_{50} IC_{50}	Non-competitive antagonist	Human Mouse	Embryonic kidney cells Neuroblastoma N1E-115 cells	Rammes, G., Rupprecht, R., Ferrari, U., Zieglgänsberger, W., & Parsons, C. G. (2001). The N-methyl-D-aspartate receptor channel blockers memantine, MRZ 2/579 and other amino-alkyl-cyclohexanes antagonise 5-HT3 receptor currents in cultured HEK-293 and N1E-115 cell systems in a non-competitive manner. *Neuroscience Letters*, *306*(1–2), 81–84. https://doi.org/10.1016/S0304-3940(01)01872-9
SERT	Serotoninergic	97,000–150,000	K_i	Weak inhibitor	Rat	Brain synaptosomes	Wesemann, W., Dette-Wildenhahn, G., & Fellehner, H. (1979). In vitro studies on the possible effects of 1-aminoadamantanes on the serotonergic system in M. Parkinson. *Journal of Neural Transmission*, *44*, 263–285. https://doi.org/10.1007/BF01250322
DAT	Dopaminergic	210,000	IC_{50}	Weak inhibitor	Rat	Striatial synaptosomes	Dunn, J. P., Henkel, J. G., & Gianutsos, G. (1986). Pharmacological activity of amantadine: Effect of N-alkyl substitution. *Journal of Pharmacy and Pharmacology*, *38*(5), 353–356. https://doi.org/10.1111/j.2042-7158.1986.tb04586.x
$\alpha_4\beta_2$	Cholinergic	8740	IC_{50}	Non-competitive antagonist	African clawed frog	Oocytes	Lee, R. H.-C., Tseng, T.-Y., Wu, C. Y.-C., Chen, P.-Y., Chen, M.-F., Kuo, J.-S., & Lee, T. J.-F. (2012). Memantine inhibits $\alpha_4\beta_4$–nAChRs-mediated nitrergic neurogenic vasodilation in porcine basilar arteries. *PLoS ONE*, *7*(7), Article e40326. https://doi.org/10.1371/journal.pone.0040326
$\alpha_4\beta_2$	Cholinergic	6600 12,510	IC_{50} IC_{50}	Non-competitive antagonist	Human African clawed frog	Embryonic kidney cells Oocytes	Buisson, B. & Bertrand, D. (1998). Open-channel blockers at the human $\alpha_4\beta_2$ neuronal nicotinic acetylcholine receptor. *Molecular Pharmacology*, *53*(3), 555–563. https://doi.org/10.1124/mol.53.3.555 Lee, R. H.-C., Tseng, T.-Y., Wu, C. Y.-C., Chen, P.-Y., Chen, M.-F., Kuo, J.-S., & Lee, T. J.-F. (2012). Memantine inhibits $\alpha_4\beta_4$–nAChRs-mediated nitrergic neurogenic vasodilation in porcine basilar arteries. *PLoS ONE*, *7*(7), Article e40326. https://doi.org/10.1371/journal.pone.0040326
α_7	Cholinergic	330–1680 at -60 to -30 mV 6000	IC_{50} IC_{50} IC_{50}	Non-competitive antagonist	Rat African clawed frog African clawed frog	Hippocampus Oocytes Oocytes	Aracava, Y., Pereira, E. F. R., Maelicke, A., & Albuquerque, E. X. (2005). Memantine blocks α_7 nicotinic acetylcholine receptors more potently than N-methyl-D-aspartate receptors in rat hippocampal neurons. *Journal of Pharmacology and Experimental Therapeutics*, *312*(3), 1195–1205. https://doi.org/10.1124/jpet.104.077172 Lee, R. H.-C., Tseng, T.-Y., Wu, C. Y.-C., Chen, P.-Y., Chen, M.-F., Kuo, J.-S., & Lee, T. J.-F. (2012). Memantine inhibits $\alpha_7\beta_4$–nAChRs-mediated nitrergic neurogenic vasodilation in porcine basilar arteries. *PLoS ONE*, *7*(7), Article e40326. https://doi.org/10.1371/journal.pone.0040326
$\alpha_9\alpha_{10}$	Cholinergic	1600	IC_{50}	Non-competitive antagonist	African clawed frog	Oocytes	Oliver, D., Ludwig, J., Reisinger, E., Zoellner, W., Ruppersberg, J. P., & Fakler, B. (2001). Memantine inhibits efferent cholinergic transmission in the cochlea by blocking nicotinic acetylcholine receptors of outer hair cells. *Molecular Pharmacology*, *60*(1), 183–189. https://doi.org/10.1124/mol.60.1.183

L-type Ca^{2+} channel	Voltage-Gated Ion Channels	445,000	IC_{50}	Antagonist	ND	Hippocampus	Parsons, C. G., Danysz, W., & Quack, G. (2001). Amino-alkyl-cyclohexanes: Uncompetitive NMDA receptor antagonists with fast, voltage-dependent blocking kinetics. https://www.researchgate.net/publication/260952655_Amino-Alkyl-Cyclohexanes_Uncompetitive_NMDA_Receptor_Antagonists_with_Fast_Voltage-Dependent_Blocking_Kinetics
$Ca_v2.2$	Voltage-Gated Ion Channels	181,000	IC_{50}	Antagonist	ND	Hippocampus	Parsons, C. G., Danysz, W., & Quack, G. (2001). Amino-alkyl-cyclohexanes: Uncompetitive NMDA receptor antagonists with fast, voltage-dependent blocking kinetics. https://www.researchgate.net/publication/260952655_Amino-Alkyl-Cyclohexanes_Uncompetitive_NMDA_Receptor_Antagonists_with_Fast_Voltage-Dependent_Blocking_Kinetics
$Ca_v2.1$	Voltage-Gated Ion Channels	360,000	IC_{50}	Antagonist	ND	Cerebellum	Parsons, C. G., Danysz, W., & Quack, G. (2001). Amino-alkyl-cyclohexanes: Uncompetitive NMDA receptor antagonists with fast, voltage-dependent blocking kinetics. https://www.researchgate.net/publication/260952655_Amino-Alkyl-Cyclohexanes_Uncompetitive_NMDA_Receptor_Antagonists_with_Fast_Voltage-Dependent_Blocking_Kinetics
TTX-resistant Na+ channel	Voltage-Gated Ion Channels	121,100	IC_{50}	Antagonist	ND	Dorsal root ganglion	Parsons, C. G., Danysz, W., & Quack, G. (2001). Amino-alkyl-cyclohexanes: Uncompetitive NMDA receptor antagonists with fast, voltage-dependent blocking kinetics. https://www.researchgate.net/publication/260952655_Amino-Alkyl-Cyclohexanes_Uncompetitive_NMDA_Receptor_Antagonists_with_Fast_Voltage-Dependent_Blocking_Kinetics
TTX-sensitive Na+ channel	Voltage-Gated Ion Channels	254,400	IC_{50}	Antagonist	ND	Dorsal root ganglion	Parsons, C. G., Danysz, W., & Quack, G. (2001). Amino-alkyl-cyclohexanes: Uncompetitive NMDA receptor antagonists with fast, voltage-dependent blocking kinetics. https://www.researchgate.net/publication/260952655_Amino-Alkyl-Cyclohexanes_Uncompetitive_NMDA_Receptor_Antagonists_with_Fast_Voltage-Dependent_Blocking_Kinetics
hERG	ND	15% at 100 µM	IP	Weak inhibitor	Chinese hamster	Ovary cells	Kambayashi, R., Goto, A., Hagiwara-Nagasawa, M., Izumi-Nakaseko,H., Shinozaki, M., Kawai, S., Matsumoto, A., Takei,Y., & Sugiyama, A. (2022). Analysis of clinically-reported, memantine-induced cardiovascular adverse responses using the halothane-anesthetized dogs: Reverse translational study. *Journal of Pharmacological Sciences*, 148(4), 343–350. https://doi.org/10.1016/j.jphs.2022.01.011
CYP2B6	Metabolic	76,700 279,700	K_i IC_{50}	Weak inhibitor	Human Human	Liver microsomes Liver microsomes	Micuda, S., Mundlova, L., Anzenbacherova, E., Anzenbacher, P., Chladek, J., Fuksa, L., & Martinkova, J. (2004). Inhibitory effects of memantine on human cytochrome P450 activities: Prediction of in vivo drug interactions. *European Journal of Clinical Pharmacology*, 60, 583–589. https://doi.org/10.1007/s00228-004-0825-1

Note:

"Value" is the measure of activity with respect to concentration. affinity, potency, or efficacy, used to determine required concentration to achieve a quantitative biological function. They're modeled by pharmacological parameters, where affinity (K_i) is the inhibition constant, antagonistic potency (IC_{50}) is the half maximal inhibitory concentration, inhibition percentage (IP) is the percent of inhibition for a specific concentration. Lower values for K_i and IC_{50} imply less concentration is needed to produce the physiological response. Higher IP implies greater inhibition at the defined oncentration.